CASE REPORT

Reversible Cerebral Vasoconstriction Syndrome without Headache

Tatsuya Tanaka, Tomihiro Wakamiya, Takahiro Kumono, Takashi Agari, Yuhei Michiwaki, Hiroshi Itokawa, Kazuaki Shimoji, Eiichi Suehiro, Keisuke Onoda, Fumitaka Yamane, and Akira Matsuno

Department of Neurosurgery, International University of Health and Welfare Narita Hospital, Chiba, Japan

Abstract : A 49-year-old woman with a family history of Moyamoya disease presented with sudden onset of right hemiparesis without headache. Magnetic resonance imaging (MRI) of the head revealed a cerebral infarct in the left corona radiata, and magnetic resonance angiography (MRA) revealed severe stenosis of the bilateral internal carotid, middle, anterior, and posterior cerebral arteries. Antithrombotic therapy improved her symptoms. After 2 weeks, MRA revealed changes in cerebral arterial vasodilation, indicating reversible cerebral vasoconstriction syndrome (RCVS). Five months later, she presented with transient dysarthria without headache ; MRA revealed multiple cerebral artery stenosis, and 2 days later, it revealed changes in cerebral arterial vasodilation. RCVS presents with reversible multifocal narrowing of the cerebral arteries with thunderclap headache, commonly observed in middle-aged women. RCVS without headache is rare. RCVS should be a differential diagnosis in patients with multiple cerebral artery stenoses without headache, and serial MRI is important for its diagnosis. J. Med. Invest. 71 : 323-326, August, 2024

Keywords **:** *reversible cerebral vasoconstriction syndrome, headache, magnetic resonance imaging, lomerizine, cerebrovascular disease*

INTRODUCTION

Reversible cerebral vasoconstriction syndrome (RCVS) is a clinical and radiological syndrome comprising several disorders characterized by sudden onset of severe headache (thunderclap headache [TCH]) and transient constriction of multiple arteries within the brain (1). Although TCH is the predominant clinical manifestation of RCVS, certain patients with RCVS may not present with the typical headache symptoms (2).

Herein, we report a patient with RCVS presenting with two ischemic strokes without headache and briefly review the current literature on RCVS without headache.

CASE REPORT

A 49-year-old female patient, with a familial history of Moyamoya disease, was transferred to our hospital because of sudden onset of right hemiparesis without headache. On hospital arrival, she had impaired consciousness (Glasgow coma scale 4-4-6). Her vital signs were as follows : blood pressure, 152/76 mmHg ; pulse rate, 93 beats per minute ; body temperature, 36.3°C ; respiratory rate, 18 breaths per minute ; and oxygen saturation, 98% on room air. Her pupils were equal (3.0 mm in diameter), round, and reactive to light. She exhibited noticeable right hemiparesis but had no meningeal signs such as nuchal rigidity, Kernig's sign, or Brudzinski's sign. Other physical and neurological examinations yielded normal results.

Laboratory tests showed a white blood cell count of 5,130/μL with 61.3% neutrophils. D-dimer (0.53 μg/mL) and C-reactive protein (0.08 mg/dL) levels were within normal ranges. The results of immunological tests, including rheumatoid factor, antinuclear antibodies, anti SS-A/SS-B antibodies, anti-neutrophil cytoplasmic antibody, anti-cardiolipin antibody, and lupus anticoagulant, we negative. Head magnetic resonance imaging (MRI) revealed a recent cerebral infarct in the left corona radiata, and magnetic resonance angiography (MRA) indicated severe stenosis in the bilateral internal carotid, middle, anterior, and posterior cerebral arteries (Figure 1A and B). Symptoms improved with antithrombotic therapy. She continued pharmacological treatment with aspirin (100 mg/day), cilostazol (200 mg/day), and rosuvastatin (5 mg/day). After 2 weeks, MRA demonstrated changes consistent with cerebral arterial vasodilation (Figure 1C), indicative of RCVS, and the patient was discharged.

Five months later, she presented with transient dysarthria but had no headache. MRA revealed multiple cerebral artery stenoses, and MRI showed no new intracranial lesions (Figure 2A). Neurological examination on admission showed no abnormal findings, and dysarthria had resolved. On day 3, MRA depicted changes in cerebral arterial vasodilation (Figure 2B). The patient had not experienced headaches during both clinical episodes. Ultimately, she was diagnosed with RCVS without headache. Pharmacological treatment continued with cilostazol (200 mg/day), rosuvastatin (5 mg/day), and lomerizine (10 mg/day). On day 5, she was neurologically intact and was discharged.

Seven months later, she remained well with no neurological deficits, and MRA revealed a cerebral arterial vasodilation (Figure 2C).

DISCUSSION

Recurrent acute severe headaches and multifocal segmental vasoconstrictions are distinctive RCVS features. The precise etiology of headaches in RCVS remains unclear ; however, a sudden alteration in central vascular tone was postulated to lead to vessel wall stretching, resulting in TCH during the initial RCVS stages (3). Our patient insisted the absence of headache during the first and second hospitalizations.

Previous studies, along with our case, have provided detailed insights into the clinical and radiological characteristics of 13 patients with RCVS who did not experience headaches (Table)

Received for publication February 15, 2024 ; accepted July 29, 2024.

Address correspondence and reprint requests to Tatsuya Tanaka, M.D., Ph. D., Department of Neurosurgery, International University of Health and Welfare, School of Medicine, Narita Hospital, 852 Hatakeda, Narita City, Chiba, Japan and E-mail : s96047@hotmail.com

(4-11). These reports delineated specific features of RCVS without headache, where all patients exhibited cerebrovascular disease concomitant with RCVS ; 12 had ischemic strokes, and one had convexity subarachnoid hemorrhage. According to Ducros *et al*., cerebral infarction was present in 6%–39% of patients with RCVS.1) RCVS without headache might be associated with a high rate of ischemic stroke. RCVS is usually triggered by specific conditions or events, including pregnancy (postpartum vasculopathy), orgasm, acute stressful or emotional situations, bathing, physical exertion, recreational drugs, or the intake of

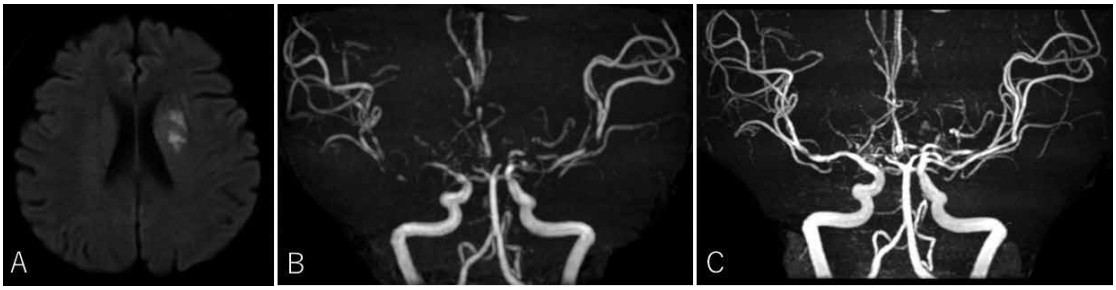

Figure 1. Initial head magnetic resonance (MR) imaging shows a cerebral infarct in the left corona radiata (A), and MR angiography (MRA) shows severe stenosis of the bilateral internal carotid, middle, anterior, and posterior cerebral arteries (B). After 2 weeks, the MRA scan shows changes in cerebral arterial vasodilation (C).

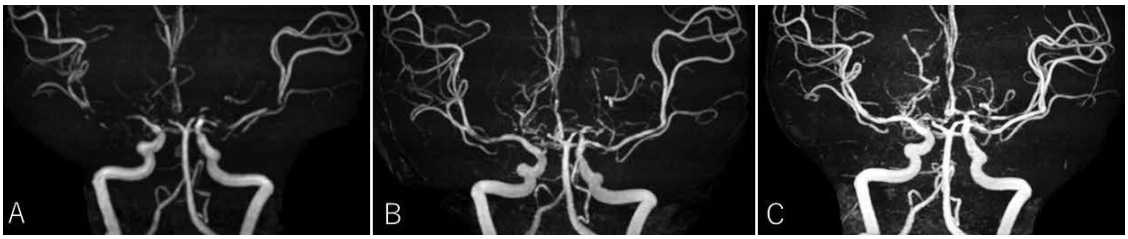

Figure 2. Magnetic resonance angiography (MRA) during the second ischemic attack shows severe stenosis of the bilateral middle, anterior, and posterior cerebral arteries (A). After 2 days, the MRA scan shows changes in cerebral arterial vasodilation (B). Seven months later, the MRA scan reveals further changes in cerebral arterial vasodilation (C).

Table. Characteristics of patients without headache associated with RCVS.

Case	Author, Year	Age/Sex	Triggers	Neurological symptoms	Complications	Outcome
1	Spitzer, 2005	24/F	Postpartum	Generalized tonic-clonic seizure	cSAH	Asymptomatic
2	Wolff, 2015	25/F	None	Diplopia, right ataxia	IS	mRS 0
3	Wolff, 2015	35/M	None	Left hemiparesis	IS	mRS 0
4	Wolff, 2015	27/M	Cannabis	Right paresthesia	IS	mRS 0
5	Wolff, 2015	38/M	Nasal decongestants	Right ataxia, dysarthria	IS	mRS 1
6	Wolff, 2015	36/M	None	Vertigo, right hemiparesis	IS	mRS 0
7	Fugate, 2012	31/F	Postpartum, Serotonergic antidepressant	Left hemiparesis	IS	Persistent deficit
8	Tsivgoulis, 2014	42/M	Cannabis	Transient episodes of right hemiparesis	IS	Asymptomatic
9	Kasuya, 2018	32/F	Pregnancy	Dizziness, diplopia	IS	mRS 0
10	Kim, 2019	46/M	None	Visual field defect, left lower limb weakness	IS	NA
11	Matsubayashi, 2021	48/M	None	First attack ; none Second attack ; convulsion Third attack ; dizziness	IS, ICH	mRS 0
12	Kakehi, 2021	81/F	Tetrodotoxin	Dysarthria, extremities weakness	IS	Asymptomatic
13	Our case	49/F	None	First attack ; Left hemiparesis Second attack ; dysarthria	IS	mRS 0

cSAH, convexity subarachnoid hemorrhage ; F, female ; ICH, intracerebral hematoma ; IS, ischemic stroke ; M, male ; mRS, modified Rankin scale ; NA, not attributable ; RCVS, reversible cerebral vasoconstriction syndrome

vasoactive drugs. There were 6 cases with no trigger for RCVS without headache, 2 cases with postpartum, 2 cases with cannabis, 1 case with pregnancy, 1 case with nasal decongestants, 1 case with serotonergic antidepressants, and 1 case with tetrodotoxin (4-11).

Moreover, the clinical outcomes of nearly all previously described patients were good and were mostly <50 years old. Our patient had common features with those patients in that no sequelae remained, and he was 49 years old.

The diagnostic criteria for RCVS proposed by Calabrese *et al*. in 2007 include the presence of severe acute headache (12). Clinically, the consideration of RCVS arises when patients experience a hyperacute severe headache, and radiological aspects become crucial in cases of RCVS without headache (2). Multiple cerebral artery stenoses are a critical RCVS feature, which is shared with various diseases, including primary angiitis of the central nervous system, secondary central nervous system vasculitis, infectious diseases, multiple embolic cerebral infarcts, anti-phospholipid antibody syndrome, and Moyamoya disease (13). In our case, laboratory tests, whole-body CT, and head MRI excluded differential diagnoses other than Moyamoya disease.

Initially, we suspected Moyamoya disease as the cause based on the MRA results and patient's family history. The recently introduced "Diagnostic Criteria 2021" for Moyamoya disease comprehensively cover various aspects, including the disease concept, diagnostic imaging, and concept of quasi-Moyamoya disease (Moyamoya syndrome) (14).

With digital subtraction angiography (DSA), MRA can also detect stenosis or occlusion of the terminal portion of the intracranial internal carotid artery and other abnormal findings of intracranial vessels and can be implemented in the diagnostic approach for Moyamoya disease (14). However, the limited diagnostic specificity of MRI and MRA poses challenges in distinguishing Moyamoya disease from other diseases. In our patient with multiple cerebral artery stenoses but without headache, serial MRI studies played an important role in the diagnostic process.

The distinctive headache is a key factor in distinguishing RCVS from Moyamoya disease. TCHs are typical in RCVS, whereas they are with hemorrhage in Moyamoya disease. However, the headache characteristic is not useful when patients do not experience it. Thus, differentiating RCVS without headache from Moyamoya disease at first consultation is challenging and may recommend revascularization surgery if symptoms or strokes develop because early treatment is important to prevent poor outcomes in Moyamoya disease. The cerebrovascular abnormality observed in our case normalized rapidly, whereas that of RCVS is often within 12 weeks. This accurate diagnosis in our case was made by meticulous follow-up.

In summary, we experienced a case involving a patient who suffered from ischemic stroke associated with RCVS. RCVS must be considered as a potential alternative diagnosis for patients who did not experience headache but exhibit multifocal segmental cerebral artery vasoconstriction on MRA. Distinguishing RCVS without headache from Moyamoya disease can be challenging initially. The subsequent clinical course may be a crucial factor in making an accurate diagnosis, and appropriate imaging should be contemplated based on the evolving clinical scenario.

CONFLICTS OF INTEREST

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

All procedures in this study were performed in accordance with the 1964 Declaration of Helsinki. A series of treatments were performed after obtaining appropriate written informed consent from the patients. The requirement for additional written consent for inclusion in this study was waived because of the retrospective and observational nature of the study.

DISCLOSURES

The authors report there are no competing interests to declare.

FUNDING

The authors have no relevant financial or nonfinancial interests to disclose.

AUTHOR CONTRIBUTIONS

TT care of patient and writing, designing, and editing of the manuscript. TW, TK, TA, YM, HI, KS, ES, KO, and F.Y. care of patient and editing of the manuscript. A.M. editing of the manuscript.

REFERENCES

1. Ducros A : Reversible cerebral vasoconstriction syndrome. Lancet Neurol 11(10) : 906-17, 2012
2. Wolff V, Ducros A : Reversible cerebral vasoconstriction syndrome without typical thunderclap headache. Headache 56(4) : 674-87, 2016
3. Chen SP, Fuh JL, Wang SJ : Reversible cerebral vasoconstriction syndrome : current and future perspectives. Expert Rev Neurother 11(9) : 1265-76, 2011
4. Wolff V, Armspach JP, Lauer V, Rouyer O, Ducros A, Marescaux C, Gény B : Ischaemic strokes with reversible vasoconstriction and without thunderclap headache : a variantof the reversible cerebral vasoconstriction syndrome? Cerebrovasc Dis 39(1) : 31-8, 2015
5. Fugate JE, Ameriso SF, Ortiz G, Schottlaender LV, Wijdicks EF, Flemming KD, Rabinstein AA : Variable presentations of postpartum angiopathy. Stroke 43(3) : 670-6, 2012
6. Spitzer C, Mull M, Rohde V, Kosinski CM : Non-traumatic cortical subarachnoid haemorrhage : diagnostic work-up and aetiological background. Neuroradiology 47 : 525-31, 2005
7. Tsivgoulis G, Lachanis S, Papathanasiou MA, Chondrogianni M, Brountzos EN, Voumvourakis K : Cannabis-associated angiopathy : an uncommon cause of crescendo transient ischemic attacks. Circulation 130(23) : 2069-70, 2014
8. Kasuya C, Suzuki M, Koda Y, Sato H, Kashima K, Honda K, Kazama Y, Akiyama K, Seki Y, Yoneoka Y : A headache-free reversible cerebral vasoconstriction syndrome (RCVS) with symptomatic brain stem ischemia at late pregnancy as a rare manifestation of RCVS resolved with termination of pregnancy by semi-urgent cesarean section. Oxf Med Case Rep 2018 : omy101, 2018
9. Kim BS, Park YK, Sunwoo MK, Yu HJ, Jeong EH, Kim DY : Is the presence of headache indispensable in diagnosing reversible cerebral vasoconstriction syndrome? J Clin Neurol 15(4) : 588-90, 2019

10. Matsubayashi T, Oniki A, Furuki M, Obayashi M : Reversible cerebral vasoconstriction syndrome without headache that was initially suspected of being primary angiitis of the central nervous system. Intern Med 60(14) : 2321-6, 2021
11. Kakehi E, Matsumoto M, Taniguchi S, Akamatsu Y, Sakurai S, Hirotani A, Nozaki T, Shoji K, Adachi S, Kotani K, Matsumura M : Reversible cerebral vasoconstriction syndrome associated with tetrodotoxin poisoning : A case report. J Am Coll Emerg Physicians Open 2(6) : e12627, 2021
12. Calabrese LH, Dodick DW, Schwedt TJ, Singhal AB : Narrative review : reversible cerebral vasoconstriction syndromes. Ann Intern Med 146(1) : 34-44, 2007
13. Hajj-Ali RA, Calabrese LH : Diagnosis and classification of central nervous system vasculitis. J Autoimmun 48 : 149-52, 2014
14. Kuroda S, Fujimura M, Takahashi J, Kataoka H, Ogasawara K, Iwama T, Tominaga T, Miyamoto S ; Research Committee on Moyamoya Disease (Spontaneous Occlusion of Circle of Willis) of the Ministry of Health, Labor, and Welfare, Japan : Diagnostic criteria for Moyamoya disease - 2021 Revised Version. Neurol Med Chir (Tokyo) 62(7) : 307-12, 2022